REMARKS

In reply to the Office Action dated May 12, 2004, claims 11-13 are currently under examination in the Application. By the above amendment, claim 12 has been canceled and claim 13 has been amended solely to remove reference to canceled claim 12. No new matter has been added. The above amendment is not to be construed as acquiescence to the stated grounds for objection/rejection and is made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Rejections under 35 U.S.C. § 102(e)

Claims 12 stands rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Jager *et al.* (WO 01/47959 A2). In particular, the Action contends that Jager *et al.* teaches the immunotherapeutic treatment of a patient comprising administering a polypeptide comprising at least 20 contiguous amino acids of the polypeptide set forth in SEQ ID NO:475.

Without acquiescing to the rejection, Applicants have canceled claim 12 without prejudice and solely to advance prosecution. Applicants reserve the right to prosecute any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Rejections under 35 U.S.C. § 112, first paragraph (written description)

Claims 11-13 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time the application was filed, had possession of the claimed invention. In particular, the Action contends that insufficient guidance is provided as to which 10% of SEQ ID NO:475 may be deleted, substituted or inserted, such that a polypeptide having at least 90% identity to SEQ ID NO:475 is produced wherein said polypeptide is useful for producing an immune response.

Applicants traverse the rejection and respectfully submit that the courts have held that all that is required to comply with the written description requirement of 35 U.S.C. § 112, first paragraph, is that the specification *reasonably convey* to a person skilled in the art that, at the time of filing, the inventor had possession of the subject matter that is claimed in the application. (*In re Edwards*, 568 F.2d 1349, 1351, 196 USPQ 465, 467 (CCPA 1978). Further, the U.S.P.T.O. has indicated that that which is conventional or well known to one of ordinary skill in the art need not be described in detail (see *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement* – Federal Register: January 5, 2001 (Volume 66, No. 4, page 1106, first column).

Applicants submit that the skilled artisan would readily appreciate that, as filed, the present specification *reasonably conveys* that Applicants were in possession of the subject matter encompassed by the claims as amended herewith. In particular, the specification clearly describes the B726P breast tumor antigen. Further, the specification as filed clearly describes generating cytotoxic T cell (CTL) lines and CD4+ T helper cell lines using the B726P polypeptide and fragments thereof (see Examples 4 and 5, pages 133-136). Additionally, the specification describes that the CTL lines generated were restricted by the HLA-B*1501 MHC class I molecule (page 133, lines 25-27). Moreover, in Examples 14 and 15 (pages 150-153), the specification describes antibody epitope mapping and specifically describes antibody epitope sequences (see Table 3, page 151 and page 152, SEQ ID NOs:597, 609, 612, 615, and 617).

Applicants submit that the skilled artisan would immediately appreciate in view of the guidance provided in the specification as filed that polypeptides with structural similarity to B726P could easily be used to generate T cells and antibodies that recognize the B726P polypeptide set forth in SEQ ID NO:475. Further, the skilled artisan would understand that such polypeptides could be generated using assays known in the art with the guidance set forth in the specification as filed. For example, the skilled artisan would immediately understand that polypeptides having 90% identity to B726P could include polypeptides that have substitutions in those amino acids predicted to bind to HLA-B*15, as described in Example 4 and the reference cited therein (*J. Immunol.*1999,*162*:7277-84) such that binding to the MHC molecule is preserved or enhanced. Alternatively, the skilled artisan would recognize that substitutions

could, for example, be located at positions outside of the binding epitope such that B*1501 epitopes are not changed. Likewise, the skilled artisan would immediately understand that polypeptides having 90% identity to B726P could include polypeptides that have substitutions outside of the antibody epitopes so that antibody reactivity is maintained. Such polypeptides could easily be generated using standard molecular biological tools known in the art, particularly in view of the teachings of the specification and immunologic reactivity could easily be tested using assays such as those described in the specification as filed (see for example page 40, lines 4-13). Thus, Applicants submit that the skilled artisan would readily appreciate that, the specification as filed provides adequate guidance as to which amino acids of SEQ ID NO:475 could be modified. Moreover, the skilled artisan would agree that the specification as filed *reasonably conveys* that Applicants were in possession of polypeptides having 90% identity to the B726P polypeptide set forth in SEQ ID NO:475 wherein said polypeptides are immunologically reactive with an antibody and/or T cell that reacts with the polypeptide set forth in SEQ ID NO:475 polypeptides. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph (enablement)

Claims 11-13 stand rejected under 35 U.S.C. § 112, first paragraph, as subject matter which was allegedly not described in the specification in such a way as to enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Action contends that Applicants arguments filed June 5, 2003 are based solely on prophetic teachings in the specification as filed. Further, the Action alleges that there is no elucidation of the actual function of the polypeptide within the breast cancer tissue. Additionally, the Action asserts that there is no evidence that stimulating antibodies would lead to the production of treatment effects specifically correlated with the treatment of breast cancer as it relates to the expression of the polypeptide of the present invention. To support this position, the Action cites Gura (Science, 1997, 278:1041-1042) as evidence that many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy. The Action further cites Hartwell *et al.* (Science, 1997, 278:1064-1068) to support the position that the specification does not provide

adequate teaching with regard to biological stability, half-life or clearance from the blood of the recited polypeptides. Thus, the Action concludes that the specification does not provide adequate guidance to make and use the claimed invention without undue experimentation.

Applicants respectfully traverse the rejection on the following grounds.

With regard to Applicants arguments filed June 5, 2003, Applicants respectfully submit that their response referenced, among others, Examples 4 and 5 of the specification as filed which, contrary to the Action's assertions, describe *in vitro* experiments carried out by Applicants. The experiments described in Example 4 show that the claimed polypeptide can induce cytotoxic T cells (CTLs) (see for example page 133, lines 14-27). Importantly, the experiments further show that the B726P-specific CTL can recognize and lyse breast tumor cells expressing B726P (see page 135, lines 1-4). Example 5 shows the generation of B726P-specific CD4+ T cell lines and further, identifies specific, naturally processed epitopes recognized by these T cell lines. Applicants respectfully submit that the skilled artisan would readily appreciate, given the experimental evidence provided in the specification as filed, that the recited polypeptide comprising SEQ ID NO:475 could be specifically useful for the immunotherapeutic treatment of breast cancer.

Concerning the actual function of the polypeptide within the breast cancer tissue, Applicants submit that such activity is not a relevant inquiry to the present claims directed to the use of the polypeptide as an immunogen. This would be readily recognized by the skilled artisan, particularly in view of the above-referenced experiments showing that CTL can be generated using the recited polypeptide that specifically recognize and kill cells expressing said polypeptide.

With regard to the Action's assertion that there is no evidence that stimulating antibodies would lead to the production of treatment effects specifically correlated with the treatment of breast cancer as it relates to the expression of the polypeptide of the present invention, Applicants submit that methods for stimulating an immune response include not only methods for stimulating an antibody response but also methods for stimulating cell mediated responses. Furthermore, Applicants submit that, to the extent the Examiner's argument is based upon a lack of evidence demonstrating therapeutic effectiveness in humans, it is respectfully

submitted that a demonstration of therapeutic efficacy in humans is not required. Applicants note that the Patent Office has explicitly adopted the position established by the courts that an applicant does not have to provide actual evidence of success in treating humans where such utility is asserted. M.P.E.P. § 2107.03(I). In addition, the M.P.E.P. enunciates the Patent Office's standard for establishing therapeutic utility when stating that "if reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process." M.P.E.P. § 2107.03(III). In *no* case has a Federal court required an applicant to support an asserted utility with data from human clinical trials. Moreover, in *In re Brana*, the Federal Circuit emphatically rejected the PTO position that human clinical testing is necessary to establish practical utility for an antitumor agent. 51 F.3d 1560. Importantly, the Court noted, citing *In re Krimmel*, 130 U.S.P.Q. 205 (C.C.P.A. 1961):

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans.

Applicants note that while certain of these cases may be primarily directed to the utility requirement under Section 101, their holdings are applicable to the enablement requirement under Section 112, as noted in M.P.E.P. § 2164.06(a)(III). Accordingly, Applicants submit that the demonstration of efficacy in generating CTL and T helper cell lines and, importantly, efficacy in killing breast tumor cells expressing the recited B726P polypeptide establishes enablement of the claimed methods for stimulating an immune response. Applicants respectfully request withdrawal of the rejection.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all the claims remaining in the application are now believed allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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